## ATTORNEY DOCKET NO. 44921-5038-US

Application No. 09/917,800

## In the claims:

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Claims 1-54 (Canceled)



- A method of predicting at least one toxic effect of a test 55. (currently amended) compound, comprising:
- preparing a gene expression profile from a <u>liver</u> cell or tissue sample (a) exposed to the test compound; and
- comparing the gene expression profile to a database comprising (b) quantitative gene expression information from a liver cell or tissue sample that has been exposed to at least one toxin and quantitative gene expression information from a control liver cell or tissue sample exposed to the toxin excipient, thereby predicting at least one toxic effect of the test compound.
- A method of claim 55, wherein the toxin is selected from 56. (previously presented) the group consisting of amitryptiline, ANIT, acetaminophen, carbon tetrachloride, cyproterone acetate, diclofenac, estradiol, indomethacin, valproate, and WY-14643.
- A method of claim 56, wherein the database comprises 57. (previously presented) quantitative gene expression information from liver cell or tissue samples that have been exposed to amitryptiline, ANIT, acetaminophen, carbon tetrachloride, cyproterone acetate, diclofenac, estradiol, indomethacin, valproate, and WY-1464.
- A method of claim 55, wherein the database comprises 58. (currently amended) quantitative gene expression information for at least one gene [that's] whose expression is correlated in the database with a hepatitis liver pathology.
- A method of claim 55, wherein the database comprises 59. (currently amended) quantitative gene expression information for at least one gene [that's] whose expression is

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correlated in the database with liver necrosis without fatty liver pathology.

- A method of claim 55, wherein the database comprises 60. (currently amended) quantitative gene expression information for at least one gene [that's] whose expression is correlated in the database with liver necrosis with fatty liver pathology.
- 61. (currently amended) A method of claim 55, wherein the database comprises quantitative gene expression information for at least one gene [that's] whose expression is correlated in the database with a liver pathology induced by a toxin that [is a] forms protein adducts [former].
- A method of claim 55, wherein step (b) comprises 62. (currently amended) comparing the expression level for at least one gene in the expression profile to the mean expression level for that gene in the [database] toxin-exposed cell or tissue samples.
- A method of claim 55, wherein step (b) further comprises 63. (currently amended) comparing the expression level for at least one gene in the expression profile to the mean expression level for that gene in the control samples.
- A method of claim 55, wherein the gene expression profile 64. (currently amended) comprises the expression level for at least one gene from a cell or tissue sample exposed to the test compound.
- A method of claim 55, wherein the gene expression profile 65. (previously presented) comprises the expression level for at least about ten genes from a cell or tissue sample exposed to the test compound.
- 66. (currently amended) A method of claim 55, wherein the gene expression profile comprises the expression level for at least about 50 genes from a cell or tissue sample exposed to

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the test compound.

- A method of claim 55, wherein the gene expression profile 67. (currently amended) comprises the expression level for at least about 100 genes from a cell or tissue sample exposed to the test compound.
- A method of claim 55, wherein the gene expression profile 68. (currently amended) is produced by hybridization of nucleic acids from a cell or tissue sample exposed to the test compound to a nucleic acid microarray.
- A method of claim 55, wherein the quantitative gene 69. (previously presented) expression in the database is produced from hybridization of nucleic acids from a liver cell or tissue sample that has been exposed to at least one toxin to a nucleic acid microarray.
- A method of claim 55, wherein the gene expression profile 70. (currently amended) is produced by quantitative or semi-quantitative amplification of cDNA corresponding to mRNA from a cell or tissue sample exposed to the test compound.
- 71. (currently amended) A method of claim 55, wherein the toxic effect is selected from the group consisting of liver damage induced by hepatitis, liver damage induced by NSAIDS, liver necrosis with fatty liver, liver necrosis without fatty liver and liver damage induced by compounds that form protein adducts [formers].
- A method of claim 55, wherein the toxic effect is 72. (previously presented) substantially similar to that induced by a toxin selected from the group consisting of amitryptiline, ANIT, acetaminophen, carbon tetrachloride, cyproterone acetate, diclofenac, estradiol, indomethacin, valproate, and WY-1464.
  - A method of claim 55, wherein the database comprises 73. (previously presented)

quantitative gene expression information for at least about 10 genes.

- 74. (previously presented) A method of claim 55, wherein the database comprises quantitative gene expression information for at least about 100 genes.
- 75. (previously presented) A method of claim 55, wherein the database further comprises sequence information for the genes in the database.
- 76. (previously presented) A method of claim 55, wherein the database further comprises descriptive information from an external database which correlates the genes in the database to the records in the external database.
- 77. (currently amended) A method of claim 55, wherein the database comprises mean expression values from liver cell or tissue samples that have been exposed to at least one toxin and mean expression values from control liver cell or tissue samples that have [not] been exposed to [a toxin] the excipient.
- 78. (previously presented) A method of claim 77, wherein the database comprises at least part of the information in Tables 3A-3S.
- 79. (previously presented) A method of claim 77, wherein the database comprises substantially all of the information in Tables 3A-3S.
- 80. (previously presented) A method of claim 77, wherein the database comprises all of the information in Tables 3A-3S.
- 81. (currently amended) A method of claim 77, wherein the database further comprises information that [measures] <u>quantifies</u> the ability of each gene to predict whether or not a sample has been exposed to a toxin.

- 82. (previously presented) A method of claim 81, wherein the information comprises a linear discriminant analysis score for each gene.
- 83. (previously presented) A method of claim 77, wherein the mean values are derived from average difference values calculated for each gene averaged across the liver cell or tissue samples that have not been exposed to a toxin or a control.
- 84. (previously presented) A method of claim 55, wherein the toxic effect comprises modulation of a metabolic pathway of Table 1.
- 85. (previously presented) A method of claim 55, wherein the toxicity is hepatotoxicity.
- 86. (currently amended) A method of predicting the hepatotoxicity of a <u>test</u> compound, comprising:
- (a) preparing a gene expression profile from a liver cell or tissue sample exposed to the test compound; and
- (b) comparing the gene expression profile to a database comprising quantitative gene expression information from a liver cell or tissue sample that has been exposed to at least one hepatotoxin and quantitative gene expression information from a control liver cell or tissue sample exposed to the toxin excipient, thereby predicting the hepatoxicity of the test compound.
- 87. (previously presented) A method of claim 86, wherein the toxin is selected from the group consisting of amitryptiline, ANIT, acetaminophen, carbon tetrachloride, cyproterone acetate, diclofenac, estradiol, indomethacin, valproate, and WY-14643.
  - 88. (currently amended) A method of predicting the hepatotoxicity of a <u>test</u>

compound, comprising:

- (a) preparing a gene expression profile from a liver cell or tissue sample exposed to the <u>test</u> compound; and
- (b) comparing the gene expression profile to a database comprising quantitative gene expression information from a liver cell or tissue sample that has been exposed to at least one hepatoxin selected from the group consisting of amitryptiline, ANIT, acetaminophen, carbon tetrachloride, cyproterone acetate, diclofenac, estradiol, indomethacin, valproate, and WY-14643 and quantitative gene expression information from a control liver cell or tissue sample exposed to the toxin excipient, thereby predicting the hepatoxicity of the test compound.
- 89. (previously presented) A method of claim 55, 82 or 84, wherein the cell sample comprises hepatocytes.
- 90. (withdrawn) A nucleic acid array for predicting at least one toxic effect of a compound, wherein the nucleic acids are identified by a process comprising identifying genes that are differentially expressed in a cell or tissue sample exposed to a hepatotoxin selected from the group consisting of amitryptiline, ANIT, acetaminophen, carbon tetrachloride, cyproterone, acetate, diclofenac, estradiol, indomethacin, valproate, and WY-14643.
- 91. (withdrawn) A kit for predicting at least one toxic effect of a compound, the kit comprising a nucleic acid array of claim 90.